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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/877,695	06/08/2001	John R. Desjarlais	16380-002001	8902
26161	7590	09/12/2005	EXAMINER	
FISH & RICHARDSON PC P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			MORAN, MARJORIE A	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 09/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/877,695

Applicant(s)

DESJARLAIS, JOHN R.

Examiner

Marjorie A. Moran

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 June 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7, 14-18, 38-50, 60, 61, 65, 67 and 68 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 14-18, 38-50, 60-61, 65, and 67-68 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/23/05 has been entered.

Election/Restriction

Based on a search of the prior art, the examiner determined that the subject matter of claims 15 and 17 do not require additional search, therefore claims 15 and 17 are hereby rejoined with the elected claims.

An action on the merits of elected claims 1-7, 14-18, 38-50, 60-61, 65, and 67-68 follows. Rejections not reiterated below are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicant's arguments filed 5/23/05 have been fully considered but they are not persuasive. The arguments are addressed below.

Claims 39-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. A method of generating a probability matrix wherein a library of proteins is then synthesized, as recited in amended claims 39 and 40, is new matter.

Original claims 39-40 limited a library to be "designed by" various procedures. It was unclear what structural limitation of the library elements was intended by the "design" limitations or if further method steps were intended, as previously set forth. Original claims 9 and 10 recited "generating" a protein sequence or combinatorial library, but nowhere did the original claims recite "generating and synthesizing" a library of sequences. The originally filed specification, on pages 6-7, discloses that "the designed proteins" designed by the inventive method may be synthesized, but does not teach synthesis of a library based on the parameters recited in the claims anywhere. Pages 30-31 of the originally filed specification describe designing libraries by increasing the upper limit on free energy or by incrementing lower probabilities for amino acids, but does not disclose actual synthesis of those libraries. Original Figure 2 provides support for designing a protein sequence or library, but does not provide support for a synthesis step. It is noted that the steps of "producing" either a single protein or a library of proteins, as recited in claims 3, 60-61, and 68 are interpreted to be steps of "generating", equivalent to those of original claims 9-10.

In response to the argument that the examiner recommended specific claim language which is now incorporated, it is noted that the previous office action stated that, "The originally filed specification discloses and exemplifies designing and generating proteins and combinatorial libraries" but did NOT specifically suggest claim limitations, specifically a limitation for "generating *and synthesizing*" a library of proteins for claims 39 and 40. As the originally filed disclosure fails to support the newly added limitations of claims 39-40, as set forth above, the claims are rejected for reciting new matter.

With regard to claim 48, although the amendment has overcome the rejection under 35 USC 112, 2nd paragraph, applicant has not provided support for the newly recited limitation of screening or selecting proteins from a library "for a desired property". The specification is silent with regard to particular properties to be screened for or against. Screening or selecting for a desired property is not inherent in either a screening or selection step, as one may screen or select AGAINST undesired properties without specifying a particular desired property. As the newly recited limitation is not supported by the originally filed disclosure, claim 48 is rejected for reciting new matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 14-16, 18, 38-50, 60-61, 65, and 67-68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 65 each recites a step of providing an ensemble of related backbone structures, and a step of applying a protein design algorithm, but fails to recite any relationship between the first and second steps. It is noted that the backbone structures are not limited to be protein or peptide "structures", however as the third step recites sampling and evaluating energetic fitness of amino acids in positions in "at least one backbone structure", it is clear that the "backbone structure" of the first step necessarily comprises amino acids and the ensemble must therefore be one of related protein or peptide backbone structures. Also, as the "sampling" (claim 1) and "generating" (claims 1 and 65) steps recite "backbone structure" limitations, it is clear that these steps are related to the first "providing" step. However, no clear relationship is recited between the step of "applying a protein design algorithm" and any other step of the claims. As the relationship between steps is unclear, the claims are indefinite.

Claim Rejections - 35 USC § 102

Claim Rejections - 35 USC § 102

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-6, 15-17, 44, 48, 60-61, 65, 67-68 are rejected under 35 U.S.C. 102(e) as being anticipated by MAYO et al. (US 6,269,312, filed 4/10/1998).

Applicant's arguments with respect to claims 1-6, 15, 48, 60-61, 65, 67-68 have been considered but are moot in view of the new ground(s) of rejection.

MAYO teaches a computerized method wherein an ensemble of backbone structures derived from a naturally occurring protein is provided, a protein design algorithm is applied, energetic fitness of various amino acid residues is evaluated, and a probability matrix is generated (col. 61, line 43-col. 70 and col. 22, lines 30-39), thereby anticipating claims 1, 6, 65 and 67. MAYO teaches specific energies for evaluation, DEE computation (col. 2, lines 34-42), and Monte Carlo simulation (col. 56), thus further anticipating claims 1 and 67, and also anticipating claim 5. MAYO teaches that his sampling and evaluating steps may be preformed iteratively (col. 6, lines 28-36), thus anticipating claim 4. MAYO teaches that particular amino acid positions may be fixed (col. 111, line 54-col. 12, line 8), thus anticipating claim 44. MAYO teaches that his backbone structure ensemble is derived from an NMR structure (col. 61, lines 64-67), or may be generated by Molecular dynamics or Monte Carlo simulation (col. 11, lines 7-17), thereby anticipating claims 15-17. MAYO teaches both generation and synthesis of either a single, optimized structure (sequence) and a rank ordered list of sequences based on his calculations (col. 2, lines 44-48 and col. 6, lines 34-42), thus anticipating claims 2-3, 60-61, and 68. MAYO's selection of an optimized structure is inherently selection for a "desired property", therefore claim 48 is anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 7, 14, 18, 38-47, 49-50, rejected under 35 U.S.C. 103(a) as being unpatentable over MAYO et al. as applied to claims 1-6, 15-17, 48, 60-61, 65, 67-68 above, in view of KOEHL et al. (J. Molec. Biol. (1994) vol. 239, pp. 249-275).

MAYO teaches a computerized method of protein design, as set forth above. MAYO further teaches that his method may be used to design proteins or enzymes with altered specificity and to evaluate mutations for particular (desired or undesired) properties (col. 11, line 60-col. 12, line 37) . MAYO also teaches generation of related backbone structures by iterative alteration (col. 11, lines 1-20), thus suggesting generation by comparative modeling and use of "families" of backbone structures. MAYO further teaches calculation and scaling of energies, calculation of a lowest energy, and generation of an optimal combination of rotamers (col's 21-22), thus suggesting an upper limit on free energy and achievement of a "desired" complexity. MAYO does not teach combining information from multiple probability matrices.

KOEHL teaches a computerized method of generating a global conformational (probability) matrix representing a protein structure (p. 250) wherein a self consistent mean field theory/algorithm (SCFM) is used to generate possible side chain sequences

and to evaluate fitness (potential energy) of all possible rotamers to generate the matrix (pp. 251-252 and 256-257). KOEHL further teaches that her matrix calculations comprise information from partition functions (p. 254) and comprise information for all amino acids (p. 259, esp. Table 3). KOEHL teaches that her method steps may be iterated in multiple cycles, using multiple matrices, until convergence is reached (e.g.; p. 254), and teaches addition and subtraction of free energy to meet accuracy constraints (pp. 254-258).

It would have been obvious to one of ordinary skill in the art at the time of invention to have incorporated the multiple matrices and information for all amino acids of KOEHL in the method of MAYO for predicting protein structures/sequences where the motivation would have been to optimize prediction of side-chain structure, as taught by KOEHL (abstract).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571) 272-0720. The examiner can normally be reached on Mon,Wed: 7-1:30; Tue,Thur: 7:30-6; Fri 7-3:30 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1631

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marjorie A. Moran
Primary Examiner
Art Unit 1631

Marjorie A. Moran
9/6/05